



pulmonary veno-occlusive disease

Pulmonary veno-occlusive disease (PVOD) is characterized by the blockage (occlusion) of the blood vessels that carry oxygen-rich (oxygenated) blood from the lungs to the heart (the pulmonary veins). The occlusion is caused by a buildup of abnormal fibrous tissue in the small veins in the lungs, which narrows the vessels and impairs blood flow. Because blood flow through the lungs is difficult, pressure rises in the vessels that carry blood that needs to be oxygenated to the lungs from the heart (the pulmonary arteries). Increased pressure in these vessels is known as pulmonary arterial hypertension.

The problems with blood flow in PVOD also impair the delivery of oxygenated blood to the rest of the body, which leads to the signs and symptoms of the condition. Shortness of breath (dyspnea) and tiredness (fatigue) during exertion are the most common symptoms of this condition. Other common features include dizziness, a lack of energy (lethargy), difficulty breathing when lying down, and a cough that does not go away. As the condition worsens, affected individuals can develop a bluish tint to the skin (cyanosis), chest pains, fainting spells, and an accumulation of fluid in the lungs (pulmonary edema).

Certain features commonly seen in people with PVOD can be identified using a test called a CT scan. One of these features, which is seen in the lungs of affected individuals, is an abnormality described as centrilobular ground-glass opacities. Affected individuals also have abnormal thickening of certain tissues in the lungs, which is described as septal lines. In addition, lymph nodes in the chest (mediastinal lymph nodes) are abnormally enlarged in people with PVOD.

PVOD can begin at any age, and the blood flow problems worsen over time. Because of the increased blood pressure in the pulmonary arteries, the heart must work harder than normal to pump blood to the lungs, which can eventually lead to fatal heart failure. Most people with this severe disorder do not live more than 2 years after diagnosis.

Frequency

The exact prevalence of PVOD is unknown. Many cases are likely misdiagnosed as idiopathic pulmonary arterial hypertension, which is increased blood pressure in the pulmonary arteries without a known cause. Research suggests that 5 to 25 percent of people diagnosed with idiopathic pulmonary arterial hypertension have PVOD. Based on these numbers, PVOD is thought to affect an estimated 1 to 2 per 10 million people.

Genetic Changes

The primary genetic cause of PVOD is mutations in the *EIF2AK4* gene. Mutations in other genes may cause a small percentage of cases. Other suspected causes of PVOD

include viral infection and exposure to toxic chemicals, including certain chemotherapy drugs.

The protein produced from the *EIF2AK4* gene helps cells respond appropriately to changes that could damage the cell. For example, when the level of protein building blocks (amino acids) in a cell falls too low, the activity of the EIF2AK4 protein helps reduce the production of other proteins, which conserves amino acids. The *EIF2AK4* gene mutations involved in PVOD likely eliminate functional EIF2AK4 protein; however, it is unknown how absence of this protein's function leads to the pulmonary vessel abnormalities that underlie PVOD.

Inheritance Pattern

When caused by mutations in the *EIF2AK4* gene, PVOD is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

In contrast, when caused by mutations in another gene, the condition can have an autosomal dominant pattern of inheritance, which means one copy of the altered gene in each cell is sufficient to cause the disorder. In these cases, one parent of an affected individual typically has increased blood pressure in the vessels of the lungs.

Other Names for This Condition

- isolated pulmonary venous sclerosis
- obstructive disease of the pulmonary veins
- pulmonary venoocclusive disease
- PVOD
- venous form of primary pulmonary hypertension

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Pulmonary veno-occlusive disease
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0034091/>

General Information from MedlinePlus

- Diagnostic Tests
<https://medlineplus.gov/diagnostictests.html>
- Drug Therapy
<https://medlineplus.gov/drugtherapy.html>

- Genetic Counseling
<https://medlineplus.gov/geneticcounseling.html>
- Palliative Care
<https://medlineplus.gov/palliativecare.html>
- Surgery and Rehabilitation
<https://medlineplus.gov/surgeryandrehabilitation.html>

Additional Information & Resources

MedlinePlus

- Encyclopedia: Pulmonary Hypertension
<https://medlineplus.gov/ency/article/000112.htm>
- Encyclopedia: Pulmonary Veno-Occlusive Disease
<https://medlineplus.gov/ency/article/000075.htm>
- Health Topic: Pulmonary Hypertension
<https://medlineplus.gov/pulmonaryhypertension.html>

Genetic and Rare Diseases Information Center

- Pulmonary venoocclusive disease
<https://rarediseases.info.nih.gov/diseases/10153/pulmonary-venoocclusive-disease>

Additional NIH Resources

- National Heart Lung and Blood Institute: What is Pulmonary Hypertension?
<https://www.nhlbi.nih.gov/health/health-topics/topics/pah/>

Educational Resources

- Centers for Disease Control and Prevention: Pulmonary Hypertension Fact Sheet
https://www.cdc.gov/DHDSP/data_statistics/fact_sheets/fs_pulmonary_hypertension.htm
- Disease InfoSearch: Pulmonary venoocclusive disease
<http://www.diseaseinfosearch.org/Pulmonary+venoocclusive+disease/6097>
- MalaCards: pulmonary venoocclusive disease
http://www.malacards.org/card/pulmonary_venoocclusive_disease
- Orphanet: Pulmonary venoocclusive disease
http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=31837

Patient Support and Advocacy Resources

- American Heart Association
http://www.heart.org/HEARTORG/Conditions/HighBloodPressure/AboutHighBloodPressure/What-is-Pulmonary-Hypertension_UCM_301792_Article.jsp
- PHCentral
<http://www.phcentral.org/>
- Pulmonary Hypertension Association
<https://www.phassociation.org/sslpage.aspx?pid=197>
- RareConnect
<https://www.rareconnect.org/en/community/pulmonary-hypertension>

ClinicalTrials.gov

- ClinicalTrials.gov
<https://clinicaltrials.gov/ct2/results?cond=%22pulmonary+veno-occlusive+disease%22>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28Pulmonary+Veno-Occlusive+Disease%5BMAJR%5D%29+AND+%28pulmonary+veno-occlusive+disease%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D>

OMIM

- PULMONARY VENOOCCCLUSIVE DISEASE 1, AUTOSOMAL DOMINANT
<http://omim.org/entry/265450>
- PULMONARY VENOOCCCLUSIVE DISEASE 2, AUTOSOMAL RECESSIVE
<http://omim.org/entry/234810>

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